Welcome to STN International! Enter x:x

LOGINID:ssspta1125rxt

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:09:56 ON 30 JUL 2003

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:10:07 ON 30 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 JUL 2003 HIGHEST RN 557055-78-4
DICTIONARY FILE UPDATES: 29 JUL 2003 HIGHEST RN 557055-78-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> ecyalosporin
ECYALOSPORIN IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> e cyclosporine

E1	192		CYCLOSPORA/BI
E2	1255		CYCLOSPORIN/BI
E3	6	-->	CYCLOSPORINE/BI
E4	2		CYCLOSQU/BI
E5	2		CYCLOSQUAL/BI
E6	2		CYCLOSQUALENE/BI
E7	7		CYCLOSQUAMOSIN/BI
E8	1		CYCLOSSORB/BI
E9	6		CYCLOSTAB/BI
E10	6		CYCLOSTACHINE/BI
E11	2		CYCLOSTATINE/BI
E12	19		CYCLOSTELLETT/BI

=> s le2-e3

	12	LE2
	1164	E3
L1	0	LE2-E3
		(LE2(W)E3)

=> s e2-e3

```
          1255 CYCLOSPORIN/BI
             6 CYCLOSPORINE/BI
L2        1255 (CYCLOSPORIN/BI OR CYCLOSPORINE/BI)

=> file ca
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      17.68      17.89

FILE 'CA' ENTERED AT 11:11:28 ON 30 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 24 Jul 2003 VOL 139 ISS 5
FILE LAST UPDATED: 24 Jul 2003  (20030724/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l1
L3            0 L1

=> s l2
L4        13328 L2

=> e reperfusion
E1           32     REPERFUSING/BI
E2            1     REPERFUSINO/BI
E3        20425 --> REPERFUSION/BI
E4           17     REPERFUSIONAL/BI
E5            1     REPERFUSIONDAMAGE/BI
E6            1     REPERFUSIONOF/BI
E7           40     REPERFUSIONS/BI
E8            6     REPERFUSIVE/BI
E9            1     REPERFUSON/BI
E10           1     REPERFUSSION/BI
E11           1     REPERHYDRATION/BI
E12           1     REPERIFUSED/BI

=> s e3
L5        20425 REPERFUSION/BI

=> s l5 and l4
L6          124 L5 AND L4

=> e heart
E1            2     HEARSON/BI
E2           80     HEARST/BI
E3       266519 --> HEART/BI
```

```
E4            2     HEART004/BI
E5            1     HEART10001420/BI
E6            1     HEART10001490/BI
E7            1     HEART20000350/BI
E8            1     HEART20000990/BI
E9            1     HEART20003090/BI
E10           1     HEART20004110/BI
E11           1     HEART20004480/BI
E12           1     HEART20004920/BI

=> s e3
L7      266519 HEART/BI

=> s l7 and l6
L8           35 L7 AND L6

=> d l8 1-35

L8   ANSWER 1 OF 35  CA  COPYRIGHT 2003 ACS on STN
AN   138:385438  CA
TI   Preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as
     phosphodiesterase IV inhibitors.
IN   Eggenweiler, Hans-Michael; Wolf, Michael; Beier, Norbert; Schelling,
     Pierre; Ehring, Thomas
PA   Merck Patent Gmbh, Germany
SO   PCT Int. Appl., 114 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2003039548      A1   20030515       WO 2002-EP11351  20021010
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI EP 2001-125455    A    20011105
OS   MARPAT 138:385438
RE.CNT  4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 2 OF 35  CA  COPYRIGHT 2003 ACS on STN
AN   138:362420  CA
TI   Cyclosporine A regulates oxidative stress-induced apoptosis in
     cardiomyocytes: mechanisms via ROS generation, iNOS, and Hsp70
AU   Chen, Huei-Wen; Chien, Chiang-Ting; Yu, Sung-Liang; Lee, Yuan-Teh; Chen,
     Wen-Jone
CS   Department of Medical Research, National Taiwan University Hospital,
     Taipei, 100, Taiwan
SO   British Journal of Pharmacology (2002), 137(6), 771-781
     CODEN: BJPCBM; ISSN: 0007-1188
PB   Nature Publishing Group
DT   Journal
LA   English
```

RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 138:265340 CA
TI Sanglifehrin A Acts as a Potent Inhibitor of the Mitochondrial Permeability Transition and **Reperfusion** Injury of the **Heart** by Binding to Cyclophilin-D at a Different Site from Cyclosporin A
AU Clarke, Samantha J.; McStay, Gavin P.; Halestrap, Andrew P.
CS School of Medical Sciences, Department of Biochemistry, University of Bristol, Bristol, BS8 1TD, UK
SO Journal of Biological Chemistry (2002), 277(38), 34793-34799
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 138:231522 CA
TI Close association between the reduction in myocardial energy metabolism and infarct size: dose-response assessment of cyclosporine
AU Niemann, Claus U.; Saeed, Maythem; Akbari, Haydar; Jacobsen, Wolfgang; Benet, Leslie Z.; Christians, Uwe; Serkova, Natalie
CS Departments of Anesthesia and Perioperative Care, University of California, San Francisco, CA, USA
SO Journal of Pharmacology and Experimental Therapeutics (2002), 302(3), 1123-1128
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 138:33011 CA
TI Decreased lung ischemia-**reperfusion** injury in rats after preoperative administration of cyclosporine and tacrolimus
AU Krishnadasan, B.; Naidu, B.; Rosengart, M.; Farr, A. L.; Barnes, A.; Verrier, E. D.; Mulligan, M. S.
CS Division of Cardiothoracic Surgery, University of Washington, Seattle, WA, 98195, USA
SO Journal of Thoracic and Cardiovascular Surgery (2002), 123(4), 756-767
CODEN: JTCSAQ; ISSN: 0022-5223
PB Mosby, Inc.
DT Journal
LA English
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 137:352901 CA
TI Preparation of substituted phenanthridinones as inhibitors of poly-ADP ribose synthase (PARS)
IN Szabo, Csaba; Jagtap, Prakash; Southan, Garry; Salzman, Andrew
PA Inotek Pharamaceuticals Corporation, USA
SO U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 587,181, abandoned.
CODEN: USXXAM
DT Patent

LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6476048	B1	20021105	US 2000-602539	20000622
	US 6277990	B1	20010821	US 1999-454867	19991207
	WO 2001042219	A2	20010614	WO 2000-US42656	20001207
	WO 2001042219	A3	20011213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1237871	A2	20020911	EP 2000-992673	20001207

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	US 1999-454867	A2	19991207
	US 2000-587181	B2	20000602
	US 2000-602539	A2	20000622
	US 2000-606587	A2	20000629
	WO 2000-US42656	W	20001207

OS MARPAT 137:352901
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 137:288733 CA
TI Protection by cyclosporin A from cardiac ischemia-**reperfusion** damage
AU Popa, Radu; Salem, Leon; Schwalb, Herzl; Merin, Gideon; Borman, Joseph B.; Bar-Tana, Jacob
CS The Joseph Lunenfeld Cardiac Surgery Research Center, Hadassah University Hospital, Jerusalem, 91120, Israel
SO Experimental & Clinical Cardiology (2000), 5(2), 77-81
CODEN: ECCAF7; ISSN: 1205-6626
PB Pulsus Group Inc.
DT Journal
LA English
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 136:257245 CA
TI Methods of treating inflammatory and immune reactions and compositions therefor
IN Zhong, Z. Robert; Lucas, Alexandra; McFadden, Grant D.
PA Can.
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002026245	A2	20020404	WO 2001-CA1369	20010928

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2001091579	A5	20020408	AU 2001-91579	20010928
PRAI	US 2000-236939P	P	20000929		
	WO 2001-CA1369	W	20010928		

L8 ANSWER 9 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 135:352847 CA
TI Interleukin-1 inhibitors in the treatment of diseases
IN Sims, John E.; O'Neal, Larry F.; Connor, Timothy; Hayes, F. Ann
PA Immunex Corp., USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087328	A2	20011122	WO 2001-US15423	20010511
	WO 2001087328	A3	20020822		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 2001053764	A1	20011220	US 2001-854162	20010511
	EP 1282435	A2	20030212	EP 2001-933326	20010511

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	US 2000-203881P	P	20000512
	US 2000-222422P	P	20000801
	WO 2001-US15423	W	20010511

L8 ANSWER 10 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 135:352794 CA
TI Immunosuppressive compositions containing an immunophilin-binding compound and a ginkgolide compound, and screening method
IN Haines, David; Tosaki, Arpad; Mahmoud, Fadia F.
PA USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085206	A2	20011115	WO 2001-US14718	20010508
	WO 2001085206	A3	20021024		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1299119 A2 20030409 EP 2001-935128 20010508

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-203110P P 20000508

WO 2001-US14718 W 20010508

L8 ANSWER 11 OF 35 CA COPYRIGHT 2003 ACS on STN

AN 135:46112 CA

TI Synthesis and use of substituted phenanthridinones as inhibitors of poly-ADP ribose synthase (PARS)

IN Szabo, Csaba; Jagtap, Prakash; Southan, Garry; Salzman, Andrew L.

PA Inotek Corporation, USA

SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001042219	A2	20010614	WO 2000-US42656	20001207
WO 2001042219	A3	20011213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6277990	B1	20010821	US 1999-454867	19991207
US 6476048	B1	20021105	US 2000-602539	20000622
US 6531464	B1	20030311	US 2000-606587	20000629
EP 1237871	A2	20020911	EP 2000-992673	20001207

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 1999-454867	A2	19991207
US 2000-587181	A2	20000602
US 2000-602539	A2	20000622
US 2000-606587	A2	20000629
WO 2000-US42656	W	20001207

OS MARPAT 135:46112

L8 ANSWER 12 OF 35 CA COPYRIGHT 2003 ACS on STN

AN 134:339083 CA

TI The roles of mitochondrial permeability transition in brain ischemia

AU Kobayashi, Tohru

CS Section of Neurosurgery, Department of Neurological Disorder Division of Neurological Science, Hokkaido University Graduate School of Medicine, Sapporo, 060-8638, Japan

SO Hokkaido Igaku Zasshi (2000), 75(4), 243-252
CODEN: HOIZAK; ISSN: 0367-6102

PB Hokkaido Igakkai

DT Journal

LA Japanese

L8 ANSWER 13 OF 35 CA COPYRIGHT 2003 ACS on STN

AN 134:278791 CA

TI The role of calcineurin in ischemia preconditioning of rat **heart**

AU Li, Shu-Lian; Qi, Yong-Fen; Chen, Ya-Hong; Zhang, Ying; Wang, Xiao-Hong; Tang, Chao-Shu
CS Institute of Cardiovascular Disease Research, The First Hospital, Beijing Medical University, Beijing, 100034, Peop. Rep. China
SO Zhongguo Dongmai Yinghua Zazhi (2000), 8(2), 103-106
CODEN: ZDYZFM; ISSN: 1007-3949
PB Zhongguo Dongmai Yinghua Zazhi Bianjibu
DT Journal
LA Chinese

L8 ANSWER 14 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 133:129866 CA
TI Methods using a CCR1 antagonist for preventing graft rejection and ischemia-**reperfusion** injury
IN Hancock, Wayne W.
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000044365	A1	20000803	WO 2000-US2123	20000127
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2360672	AA	20000803	CA 2000-2360672	20000127
	EP 1152752	A1	20011114	EP 2000-907060	20000127
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002535358	T2	20021022	JP 2000-595669	20000127
PRAI	US 1999-239283	A2	19990129		
	WO 2000-US2123	W	20000127		

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 132:329637 CA
TI Protective effects of low and high doses of cyclosporin A against reoxygenation injury in isolated rat cardiomyocytes are associated with differential effects on mitochondrial calcium levels
AU Griffiths, E. J.; Ocampo, C. J.; Savage, J. S.; Stern, M. D.; Silverman, H. S.
CS Division of Cardiology, Johns Hopkins University Hospital, Baltimore, MD, USA
SO Cell Calcium (2000), 27(2), 87-95
CODEN: CECADV; ISSN: 0143-4160
PB Churchill Livingstone
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 132:160980 CA

TI Antisense oligodeoxynucleotides prevent acute cardiac allograft rejection via a novel, nontoxic, highly efficient transfection method
AU Poston, Robert S.; Mann, Michael J.; Hoyt, E. Grant; Ennen, Michael; Dzau, Victor J.; Robbins, Robert C.
CS Department of Cardiothoracic Surgery, Stanford University School of Medicine, Stanford, CA, 94305, USA
SO Transplantation (1999), 68(6), 825-832
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 132:59191 CA
TI Therapeutic methods employing disulfide derivatives of dithiocarbamates and compositions useful therefor
IN Lai, Ching-San; Vassilev, Vassil
PA Medinox, Inc., USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9966918	A1	19991229	WO 1999-US14237	19990622
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6093743	A	20000725	US 1998-103639	19980623
	CA 2335858	AA	19991229	CA 1999-2335858	19990622
	AU 9947119	A1	20000110	AU 1999-47119	19990622
	EP 1089723	A1	20010411	EP 1999-930617	19990622
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002518441	T2	20020625	JP 2000-555604	19990622
	US 6316502	B1	20011113	US 2000-565666	20000505
PRAI	US 1998-103639	A2	19980623		
	WO 1999-US14237	W	19990622		

OS MARPAT 132:59191
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 131:332966 CA
TI A process to study changes in gene expression in T lymphocytes
IN Prashar, Yatindra; Weissman, Sherman
PA Gene Logic, Inc., USA
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 9957130	A1	19991111	WO 1999-US9761	19990505
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2326827	AA	19991111	CA 1999-2326827	19990505
	AU 9938807	A1	19991123	AU 1999-38807	19990505
	AU 759785	B2	20030501		
	EP 1075485	A1	20010214	EP 1999-921657	19990505
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1998-84329P	P	19980505		
	WO 1999-US9761	W	19990505		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 131:252515 CA
TI Evidence that cyclophilin-A protects cells against oxidative stress
AU Doyle, Veronica; Virji, Sukaina; Crompton, Martin
CS Department of Biochemistry and Molecular Biology, University College London, London, WC1E 6BT, UK
SO Biochemical Journal (1999), 341(1), 127-132
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 131:153752 CA
TI Modified pharmacologically active agents with cleavable thiocarbonyl sulfide substituent and improved therapeutic methods employing them
IN Lai, Ching-San
PA Medinox, Inc., USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9940787	A1	19990819	WO 1999-US2678	19990208
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9926627	A1	19990830	AU 1999-26627	19990208
PRAI	US 1998-74694P	A1	19980213		
	WO 1999-US2678	W	19990208		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 131:139497 CA
TI Methods for the controlled delivery of carbon disulfide for the treatment

of inflammatory conditions
IN Lai, Ching-San
PA Medinox, Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9940907	A1	19990819	WO 1999-US2679	19990208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926628	A1	19990830	AU 1999-26628	19990208
PRAI US 1998-74741P	A1	19980213		
WO 1999-US2679	W	19990208		

OS MARPAT 131:139497
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 130:332527 CA
TI Reduction of infarct size in isolated rat **heart** by CsA and FK506: possible role of phosphatase inhibition
AU Cai, Qing; Baxter, Gary F.; Yellon, Derek M.
CS The Hatter Institute, UCL Hospitals and Medical School, London, WC1E 6DB, UK
SO Cardiovascular Drugs and Therapy (1998), 12(5), 499-501
CODEN: CDTHET; ISSN: 0920-3206
PB Kluwer Academic Publishers
DT Journal
LA English
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 130:261685 CA
TI Cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury in rats
AU Squadrito, Francesco; Altavilla, Domenica; Squadrito, Giovanni; Saitta, Antonino; Campo, Giuseppe M.; Arlotta, Mariarita; Quartarone, Cristina; Ferlito, Marcella; Caputi, Achille P.
CS Institute of Pharmacology, School of Medicine, University of Messina, Messina, 98121, Italy
SO European Journal of Pharmacology (1999), 364(2/3), 159-168
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 130:177253 CA
TI Cyclosporin A does not affect cardiolipin biosynthesis during ischemia-

reperfusion injury in the **heart**
AU Ross, T. K.; Hatch, G. M.
CS Department of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, MB, R3E OW3, Can.
SO Proceedings of the Western Pharmacology Society (1998), 41, 17-19
CODEN: PWPSA8; ISSN: 0083-8969
PB Western Pharmacology Society
DT Journal
LA English
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 129:239628 CA
TI Effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure
AU Jurado, F.; Bellon, J. M.; Pareja, J. A.; Golitsin, A.; Millan, L.; Pascual, G.; Bujan, J.
CS Department of Morphological Sciences and Surgery (Surgical Research Laboratory), Faculty of Medicine, University of Alcala de Henares, Madrid, 28871, Spain
SO Histology and Histopathology (1998), 13(3), 761-774
CODEN: HIHIES; ISSN: 0213-3911
PB Histology and Histopathology
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 129:156700 CA
TI Cyclosporine A limits myocardial infarct size even when administered after onset of ischemia
AU Weinbrenner, Christof; Liu, Guang S.; Downey, James M.; Cohen, Michael V.
CS University of South Alabama, MSB 3050, Departments of Physiology and Medicine, College of Medicine, Mobile, AL, 36688, USA
SO Cardiovascular Research (1998), 38(3), 676-684
CODEN: CVREAU; ISSN: 0008-6363
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 127:306090 CA
TI Cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/**reperfusion** injury
AU Halestrap, A. P.; Connern, C. P.; Griffiths, E. J.; Kerr, P. M.
CS Departments of Biochemistry and Cardiac Surgery, University of Bristol, Bristol, BS8 ITD, UK
SO Molecular and Cellular Biochemistry (1997), 174(1&2), 167-172
CODEN: MCBIB8; ISSN: 0300-8177
PB Kluwer
DT Journal
LA English

L8 ANSWER 28 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 127:13451 CA
TI Triterpene derivatives with immunosuppressant activity, their preparation, and compositions containing them

IN Baker, Robert K.; Bao, Jianming; Kayser, Frank; Parsons, William H.; Rupprecht, Kathleen M.
PA Merck and Co., Inc., USA; Baker, Robert K.; Bao, Jianming; Kayser, Frank; Parsons, William H.; Rupprecht, Kathleen M.
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9716068	A1	19970509	WO 1996-US17211	19961028
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9674781	A1	19970522	AU 1996-74781	19961028
	AU 712015	B2	19991028		
	EP 877554	A1	19981118	EP 1996-937010	19961028
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 11514648	T2	19991214	JP 1996-517439	19961028
PRAI	US 1995-8169		19951031		
	US 1995-8189		19951031		
	GB 1996-3833		19960223		
	GB 1996-5156		19960312		
	WO 1996-US17211		19961028		

OS MARPAT 127:13451

L8 ANSWER 29 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 126:338797 CA
TI Cardioprotection by cyclosporine A in experimental ischemia and **reperfusion** - evidence for a nitric oxide-dependent mechanism mediated by endothelin
AU Massoudy, P.; Zahler, S.; Kupatt, C.; Reder, E.; Becker, B. F.; Gerlach, E.
CS Dep. of Physiology and Dep. of Prophylaxis of Circulatory Diseases, Univ. of Munich, Germany
SO Journal of Molecular and Cellular Cardiology (1997), 29(2), 535-544
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic
DT Journal
LA English

L8 ANSWER 30 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 124:45225 CA
TI On the nature of the cyclosporin A binding component of the mitochondrial Ca2+-dependent pore
AU Crompton, M.; Andreeva, L.; Tanveer, A.; Leyssens, A.
CS Department Biochemistry and Molecular Biology, University College London, London, WC1E 6BT, UK
SO Progress in Cell Research (1995), 5(Thirty Years of Progress in Mitochondrial Bioenergetics and Molecular Biology), 125-8
CODEN: PRCREB; ISSN: 0924-8315
PB Elsevier
DT Journal
LA English

L8 ANSWER 31 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 120:213889 CA

TI On the involvement of a cyclosporin A sensitive mitochondrial pore in myocardial **reperfusion** injury
AU Duchen, Michael R.; McGuinness, Orla; Brown, Leslie A.; Crompton, Martin
CS Univ. Coll. London, London, WC1E 6BT, UK
SO Cardiovascular Research (1993), 27(10), 1790-4
CODEN: CVREAU; ISSN: 0008-6363
DT Journal; General Review
LA English

L8 ANSWER 32 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 120:153337 CA
TI Protection by cyclosporin A of ischemia/**reperfusion**-induced damage in isolated rat hearts
AU Griffiths, Elinor J.; Halestrap, Andrew P.
CS Sch. Med., Univ. Bristol, Bristol, BS8 1TD, UK
SO Journal of Molecular and Cellular Cardiology (1993), 25(12), 1461-9
CODEN: JMCDAY; ISSN: 0022-2828
DT Journal
LA English

L8 ANSWER 33 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 117:184589 CA
TI Impairment by cyclosporin A of **reperfusion**-induced arrhythmias
AU Arteaga, Diana; Odor, Alberto; Lopez, Rosa M.; Contreras, Gloria; Pichardo, Julieta; Garcia, Elizabeth; Aranda, Alberto; Chavez, Edmundo
CS Dep. Bioquim., Inst. Nac. Cardiol., Ignacio Chavez, Mex.
SO Life Sciences (1992), 51(14), 1127-34
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English

L8 ANSWER 34 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 113:71043 CA
TI Cyclosporin and mitochondrial dysfunction
AU McGuinness, Orla; Crompton, Martin
CS Dep. Biochem., Univ. Coll. London, London, WC1E 6BT, UK
SO Biochemical Society Transactions (1990), 18(5), 883-4
CODEN: BCSTB5; ISSN: 0300-5127
DT Journal
LA English

L8 ANSWER 35 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 112:229458 CA
TI Inhibition of calcium-induced large-amplitude swelling of liver and **heart** mitochondria by cyclosporin is probably caused by the inhibitor binding to mitochondrial-matrix peptidyl-prolyl cis-trans isomerase and preventing it interacting with the adenine nucleotide translocase
AU Halestrap, Andrew P.; Davidson, Anne M.
CS Sch. Med. Sci., Univ. Bristol, Bristol, BS8 1TD, UK
SO Biochemical Journal (1990), 268(1), 153-60
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English

=> d l8 23 all

L8 ANSWER 23 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 130:261685 CA
TI Cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury in rats

AU Squadrito, Francesco; Altavilla, Domenica; Squadrito, Giovanni; Saitta, Antonino; Campo, Giuseppe M.; Arlotta, Mariarita; Quartarone, Cristina; Ferlito, Marcella; Caputi, Achille P.

CS Institute of Pharmacology, School of Medicine, University of Messina, Messina, 98121, Italy

SO European Journal of Pharmacology (1999), 364(2/3), 159-168
CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier Science B.V.

DT Journal

LA English

CC 1-7 (Pharmacology)

AB The present study was designed to evaluate the effect of cyclosporin A in a rat model of myocardial ischemia-**reperfusion** injury (MI/R). Anesthetized rats were subjected to total occlusion (20 min) of the left main coronary artery followed by 5 h **reperfusion** (MI/R). Sham myocardial ischemia-**reperfusion** rats (Sham MI/R) were used as controls. Myocardial necrosis, myocardial myeloperoxidase activity (MPO), serum creatinine phosphokinase activity (CPK), serum tumor necrosis factor (TNF-.alpha.), cardiac mRNA for TNF-.alpha., cardiac intercellular adhesion mol.-1 (ICAM-1) immunostaining, and myocardial contractility (left ventricle dP/dtmax) were evaluated. Myocardial ischemia plus **reperfusion** in untreated rats produced marked myocardial necrosis, increased serum CPK activity and myeloperoxidase activity (a marker of leukocyte accumulation) both in the area-at-risk and in the necrotic area, reduced myocardial contractility, and induced a marked increase in the serum levels of the TNF-.alpha.. Furthermore, increased cardiac mRNA for TNF-.alpha. was measurable within 10-20 min of left main coronary artery occlusion in the area-at-risk and increased levels were generally sustained for 0.5 h. Finally, myocardial ischemia-**reperfusion** injury increased ICAM-1 staining in the myocardium. The administration of cyclosporin A (0.25, 0.5, and 1 mg/kg as an i.v. infusion 5 min after coronary artery occlusion) lowered myocardial necrosis and myeloperoxidase activity in the area-at-risk and in the necrotic area, decreased serum CPK activity, increased myocardial contractility, reduced serum levels of TNF-.alpha. and the cardiac cytokine mRNA levels, and blunted ICAM-1 immunostaining in the injured myocardium. The data suggest that cyclosporin A suppresses leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury.

ST cyclosporin A leukocyte accumulation; myocardial ischemia **reperfusion** injury cyclosporin A

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)

IT Immunosuppression
Leukocyte
Reperfusion
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)

IT Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)

IT Immunoassay
(immunol. staining; cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)

IT **Heart**, disease
(infarction; cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)

IT **Heart**, disease
(ischemia; cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT 9001-15-4, Creatinine phosphokinase 9003-99-0, Myeloperoxidase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT **59865-13-3**, Cyclosporin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Arbustini, E; Am J Cardiol 1991, V68, P368
(2) Braquet, P; Pharmacol Rev 1987, V39, P97 CA
(3) Chung, M; Circ Res 1990, V67, P753 CA
(4) Clipstone, N; Ann New York Acad Sci 1993, V696, P20 CA
(5) Coker, S; Br J Pharmacol 1985, V86, P259 CA
(6) Collart, M; Mol Cell Biol 1990, V10, P1498 CA
(7) Dzau, V; Circ Res 1993, V16(Suppl II), PII5
(8) Feuerstein, G; Prostaglandin 1984, V27, P781 CA
(9) Finkel, M; Science 1992, V257, P387 CA
(10) Fruman, D; Immunosuppressive Drugs:Developments in Anti-rejection Therapy 1994, P15
(11) Hirsh, A; Circ Res 1991, V69, P475
(12) Hsu, S; Am J Clin Pathol 1981, V75, P734 CA
(13) Klein, H; Arch Pathol Anat 1981, V393, P287 CA
(14) Lucchesi, B; Annu Rev Physiol 1990, V52, P561 CA
(15) Massoudy, P; J Mol Cell Cardiol 1977, V29, P535
(16) McCord, J; New Engl J Med 1985, V312, P159 CA
(17) McMurray, J; Br Heart J 1991, V66, P356 MEDLINE
(18) Mullane, K; J Pharmacol Methods 1985, V14, P156
(19) Schreck, R; Free Radic Res Commun 1992, V17, P221 CA
(20) Schunkert, R; J Clin Invest 1990, V86, P1913
(21) Seekamp, A; Am J Pathol 1993, V143, P464 CA
(22) Seekamp, A; Am J Pathol 1994, V144, P592 CA
(23) Shandelya, S; Circulation 1993, V88, P2812 CA
(24) Squadrito, F; Eur J Pharmacol 1993, V273, P223
(25) Squadrito, F; Inflamm Res 1996, V45, P14 CA
(26) Squadrito, F; Life Sci 1993, V53, P341 CA
(27) van der Poll, T; Shock 1995, V3, P1 MEDLINE
(28) Wiederrecht, G; Ann New York Acad Sci 1993, V696, P9 CA
(29) Wu, C; Transplantation 1990, V54, P326
(30) Yamada, T; Circulation 1994, V89, P846 CA

=> d 18 25 all

L8 ANSWER 25 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 129:239628 CA
TI Effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure

AU Jurado, F.; Bellon, J. M.; Pareja, J. A.; Golitsin, A.; Millan, L.; Pascual, G.; Bujan, J.
CS Department of Morphological Sciences and Surgery (Surgical Research Laboratory), Faculty of Medicine, University of Alcala de Henares, Madrid, 28871, Spain

SO Histology and Histopathology (1998), 13(3), 761-774

CODEN: HIHIES; ISSN: 0213-3911
PB Histology and Histopathology
DT Journal
LA English
CC 1-7 (Pharmacology)
Section cross-reference(s): 14
AB The present study investigates the effects on the cardiac muscle cell of 2 of the detg. factors for the success of organ transplant; ischemia-perfusion and immunosuppressive treatment with cyclosporin-A (CsA). To this end an abdominal, heterotopic **heart** transplant model in singenic Sprague-Dawley rats was employed. Three study groups were established: group I (control, n=15) animals undergoing **heart** transplant without treatment; group II (n=15) animals undergoing **heart** transplant and subjected to a daily dose of CsA in a cremophor vehicle (Sandimun) (5 mg/kg/s.c.); group III (n=15) animals undergoing **heart** transplant and administered a daily dose of pure CsA (5 mg/kg/s.c.). Recipient animals were sacrificed 7, 14, 21, 30, and 50 days after transplant. During the post-operative period, **heart** function was assessed by daily abdominal palpation. Graft specimens obtained at each follow-up period were subjected to light and transmission electron microscopy. Immunohistochem. anal. of specimens was performed using the rat macrophage-specific monoclonal antibody MCA-341. The ischemia/**reperfusion** process induced considerable alteration to cardiac muscle cells of control animals. Effects, apparent after the 1st week of transplant, included mitochondrial swelling and loss of cristae, hypertrophy of the sarcoplasmic reticulum and structural changes to sarcomeres. Two weeks after transplant, the myocardium was infiltrated by inflammatory cells. These effects diminished 30 days post-transplant. Cardiac tissues of treated animals (groups II and III) showed similar behavior although, in the latter group, mitochondrial damage was greater and intense myocardial fibrosis took place. Infiltration of cardiac muscle by white blood cells did not take place until 3 wk post-implant. These results indicate: a) The ultrastructural changes detected in cardiac fibers of animals of the 3 study groups were attributable to the ischemia/**reperfusion** process rather than to treatment with CsA; b) CsA appears to augment mitochondrial damage and myocardial fibrosis; c) the inflammatory response was delayed and reduced by the immunosuppressant; and d) the cremophor administration vehicle did not seem to exert an independent toxic effect on the myocardium.
ST cyclosporinA **heart** transplant ischemia **reperfusion** immunosuppressant
IT Immunosuppressants
(effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)
IT Transplant and Transplantation
(**heart**; effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)
IT **Reperfusion**
(injury; effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)
IT **Heart**
(transplant; effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)
IT 39279-69-1, Cremophor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of cyclosporin-A and its vehicle on cardiac muscle ultrastructure)
IT **59865-13-3**, Cyclosporin-A
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Abbott, C; Arch Surg 1964, V89, P645 MEDLINE
(2) Bakker, A; Histol Histopathol 1995, V10, P405 MEDLINE
(3) Bellon, J; J Biom Mater Res 1996, V31, P1 CA
(4) Bellon, J; Transplantation 1995, V60, P407 CA
(5) Bernier, M; Circ Res 1986, V58, P331 CA
(6) Bolli, R; J Am Coll Cardiol 1988, V12, P239 CA
(7) Braunwald, E; J Clin Invest 1985, V76, P1713 MEDLINE
(8) Cohen, D; Ann Intern Med 1984, V101, P667 CA
(9) de Caterina, R; Transplantation 1995, V60, P270 CA
(10) Del Maestro, R; Acta Physiol Scand (suppl) 1980, V492, P153 CA
(11) Engel, W; Nature 1961, V191, P389 MEDLINE
(12) Engler, R; Am J Physiol 1986, V251, P93
(13) Forman, M; J Am Coll Cardiol 1989, V13, P450 MEDLINE
(14) Fremes, S; J Thorac Cardiovasc Surg 1995, V110, P293 MEDLINE
(15) Garcia-Poblete, E; Histol Histopathol 1997, V12, P375 MEDLINE
(16) Guttmann, R; Transplant Proc 1994, V5, P2564
(17) Homan, W; Transplantation 1980, V30, P354 CA
(18) Hutcheson, A; Res Commun Mol Pathol Pharmacol 1995, V89, P17 CA
(19) Jeevanandam, V; J Thorac Cardiovasc Surg 1992, V104, P224 MEDLINE
(20) Kahan, B; Transplantation 1985, V40, P457 CA
(21) Karch, S; J Heart Transplant 1985, V4, P210 MEDLINE
(22) Klintmalm, G; Transplantation 1981, V32, P488 MEDLINE
(23) Luke, R; J Clin Invest 1991, V87, P1594 MEDLINE
(24) Mason, J; Pharmacol Rev 1984, V41, P423
(25) Meiser, B; Lancet 1991, V338, P1297 MEDLINE
(26) Menasche, P; J Thorac Cardiovasc Surg 1993, V105, P353 MEDLINE
(27) Millane, T; J Heart Lung Transplant 1994, V13, P473 MEDLINE
(28) Morris, P; Transplant Proc 1983, V15, P2287 CA
(29) Ono, K; J Thorac Cardiovasc Surg 1969, V57, P225 MEDLINE
(30) Paul, L; Transplantation 1994, V57, P1767 MEDLINE
(31) Pesonen, E; J Thorac Cardiovasc Surg 1995, V110, P768 MEDLINE
(32) Severs, N; Electron Microscopy 92, Eurem 92 1992, V1, P627
(33) Severs, N; Histol Histopathol 1995, V10, P481 MEDLINE
(34) Smith, J; Am J Pathol 1991, V139, P801 MEDLINE
(35) Stringham, J; J Thorac Cardiovasc Surg 1994, V107, P764 MEDLINE
(36) Tatou, E; Pharmacology 1996, V52, P1 CA
(37) Tauber, J; Transplantation 1978, V26, P409 MEDLINE
(38) Thomson, A; Immunology 1983, V48, P301 CA
(39) Uretsky, B; Circulation 1987, V76, P827 MEDLINE
(40) Wish, J; Transplant Proc 1986, V18(suppl 2), P15

=> d 18 26 all

L8 ANSWER 26 OF 35 CA COPYRIGHT 2003 ACS on STN

AN 129:156700 CA

TI Cyclosporine A limits myocardial infarct size even when administered after onset of ischemia

AU Weinbrenner, Christof; Liu, Guang S.; Downey, James M.; Cohen, Michael V.

CS University of South Alabama, MSB 3050, Departments of Physiology and Medicine, College of Medicine, Mobile, AL, 36688, USA

SO Cardiovascular Research (1998), 38(3), 676-684
CODEN: CVREAU; ISSN: 0008-6363

PB Elsevier Science B.V.

DT Journal

LA English

CC 1-8 (Pharmacology)

AB The effects of the immunosuppressant drug cyclosporin A (CsA) as a

preconditioning mimetic were examd. in rabbit hearts. CsA, a potent protein 2B or calcium/calmodulin-dependent phosphatase (PP) inhibitor, was administered to isolated rabbit hearts starting either 15 min prior to or 10 or 20 min after the onset of a 30-min regional ischemia and continuing until the onset of **reperfusion**. The effects of pretreatment with another PP2B antagonist, FK-506, were also examd. In an addnl. expt. NG-nitro-L-arginine Me ester (L-NAME) was perfused for 50 min starting 5 min before the 45-min infusion of CsA. After 2 h of **reperfusion** the infarction size was measured with the triphenyltetrazolium chloride method. In the second study, left ventricular biopsies of isolated rabbit hearts were obtained to measure the effects of CsA on the dephosphorylation of [32P]phosphorylase kinase by calcium/calmodulin-dependent phosphatases. Pretreatment with CsA resulted in only 10% infarction in the risk zone, significantly less than in untreated controls (28.7%), but comparable to the extent of infarction in ischemia preconditioned hearts (10%). Equivalent protection was also obsd. in hearts with treatment delayed for 10 min following the onset of ischemia (10.4% infarction). The protection waned when CsA was given only during the last 10 min of the 30-min ischemic period (25.5% infarction). Pretreatment with FK-506 also resulted in myocardial salvage (10.4% infarction). When the hearts were exposed to a coinfusion of L-NAME and CsA, the protection was still evident (18.1% infarction), although not as robustly as with the PP2B blocker alone. In hearts pretreated with CsA the dephosphorylation of [32P]phosphorylase kinase by calcium/calmodulin-dependent phosphatases was inhibited by 67%. Thus, CsA and FK-506, potent PP2B inhibitors, can protect the ischemic rabbit **heart**. CsA continues to be effective when its infusion is delayed until after the onset of **heart** ischemia. The mechanism of this protection may be related to the inhibition of phosphatases and prolongation of the phosphorylation state of ischemic cells.

ST **heart** ischemia infarction cyclosporine FK506 nitroarginine

IT **Heart**, disease
(infarction; cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)

IT **Heart**, disease
(ischemia; cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)

IT 50903-99-6, L-Name **59865-13-3**, Cyclosporin A 104987-11-3, Tacrolimus
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)

IT 9001-88-1, Phosphorylase kinase 9025-75-6, Protein phosphatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Armstrong, S; J Mol Cell Cardiol 1992, V24, P869 CA
(2) Armstrong, S; J Mol Cell Cardiol 1996, V28, P1479 CA
(3) Armstrong, S; J Mol Cell Cardiol 1997, V29, P3009 CA
(4) Banerjee, A; Circ Res 1993, V73, P656 CA
(5) Bilinska, M; Mol Cell Biochem 1996, V160, P265
(6) Brunner, F; J Mol Cell Cardiol 1992, V24, P1291 CA
(7) Bunchman, T; J Clin Invest 1991, V88, P310 CA
(8) Caroni, P; Soc Gen Physiol Ser 1984, V38, P149 CA
(9) Clipstone, N; Nature 1992, V357, P695 CA
(10) Cohen, M; Cardiovasc Res 1994, V28, P61 MEDLINE
(11) Crompton, M; Biochem J 1988, V255, P357 CA
(12) Duchen, M; Cardiovasc Res 1993, V27, P1790 CA

(13) Fahr, A; Clin Pharmacokinet 1993, V24, P472 MEDLINE
(14) Fruman, D; Proc Natl Acad Sci USA 1992, V89, P3686 CA
(15) Fukuda, H; Biochem Biophys Res Commun 1996, V220, P160 CA
(16) Gabauer, I; Can J Cardiol 1994, V10, P125 CA
(17) Ganapathi, M; Arch Biochem Biophys 1984, V233, P19 CA
(18) Goodall, T; J Cardiovasc Pharmacol 1995, V26(Suppl 3), PS482
(19) Goto, M; Cardiovasc Res 1991, V25, P943 CA
(20) Goto, M; Circ Res 1995, V77, P611 CA
(21) Griffiths, E; Biochem J 1991, V274, P611 CA
(22) Griffiths, E; Biochem J 1995, V307, P93 CA
(23) Griffiths, E; J Mol Cell Cardiol 1993, V25, P1461 CA
(24) Groblewski, G; J Biol Chem 1994, V269, P15111 CA
(25) Ikonomidis, J; Am J Physiol 1997, V272, PH1220 CA
(26) Kahan, B; New Engl J Med 1989, V321, P1725 CA
(27) Klee, C; Methods Enzymol 1983, V102, P227 CA
(28) Laemmli, U; Nature 1970, V227, P680 CA
(29) Linden, J; Trends Pharmacol Sci 1994, V15, P298 CA
(30) Liu, G; Circulation 1991, V84, P350 CA
(31) Liu, J; Cell 1991, V66, P807 CA
(32) Liu, Y; Cardiovasc Drugs Ther 1994, V8, P881 MEDLINE
(33) Liu, Y; Circ Res 1996, V78, P443 CA
(34) Liu, Y; J Mol Cell Cardiol 1995, V27, P883 CA
(35) Massoudy, P; J Mol Cell Cardiol 1997, V29, P535 CA
(36) Maxwell, M; Cardiovasc Res 1987, V21, P737 MEDLINE
(37) Murry, C; Circulation 1986, V74, P1124 MEDLINE
(38) Schreiber, S; Immunol Today 1992, V13, P136 CA
(39) Schultz, J; Am J Physiol 1995, V268, PH2157 CA
(40) Speechly-Dick, M; Circ Res 1994, V75, P586 CA
(41) Stewart, A; Eur J Biochem 1981, V115, P197 CA
(42) Stewart, A; Eur J Biochem 1983, V132, P289 CA
(43) Stewart, A; FEBS Lett 1982, V137, P80 CA
(44) Stewart, A; Methods Enzymol 1988, V159, P409 CA
(45) Takeda, Y; J Cardiovasc Pharmacol 1993, V22(Suppl 8), PS310
(46) Taniguchi, I; J Mol Cell Cardiol 1997, V29, PA232
(47) Thornton, J; Circulation 1992, V85, P659 CA
(48) Thornton, J; J Mol Cell Cardiol 1993, V25, P311 CA
(49) Tsuchida, A; Circ Res 1994, V75, P576 CA
(50) Vander, H; Cardiovasc Res 1996, V31, P711
(51) Walsh, A; FEBS Lett 1997, V416, P230 CA
(52) Walsh, C; J Biol Chem 1992, V267, P13115 CA
(53) Wang, P; Basic Res Cardiol 1996, V91, P458 MEDLINE
(54) Wang, P; J Mol Cell Cardiol 1996, V28, P579 CA
(55) Weinbrenner, C; Circulation, in press 1998
(56) Weinbrenner, C; J Mol Cell Cardiol 1997, V29, P2383 CA
(57) Wera, S; Biochem J 1995, V311, P17 CA
(58) Weselcouch, E; Am J Physiol 1995, V268, PH242 CA
(59) Wolf, H; Proc Natl Acad Sci USA 1980, V77, P5852 CA
(60) Woolfson, R; Circulation 1995, V91, P1545 CA
(61) Yang, X; J Mol Cell Cardiol 1997, V29, P991 CA
(62) Yao, Z; Am J Physiol 1993, V264, PH2221 CA
(63) Ytrehus, K; Am J Physiol 1994, V266, PH1145 CA
(64) Zimmermann, N; Transplant Proc 1994, V26, P2875 CA

=> d l8 27 all

L8 ANSWER 27 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 127:306090 CA
TI Cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/**reperfusion** injury
AU Halestrap, A. P.; Connern, C. P.; Griffiths, E. J.; Kerr, P. M.

CS Departments of Biochemistry and Cardiac Surgery, University of Bristol, Bristol, BS8 ITD, UK

SO Molecular and Cellular Biochemistry (1997), 174(1&2), 167-172
CODEN: MCBIB8; ISSN: 0300-8177
PB Kluwer
DT Journal
LA English
CC 14-5 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1

AB When loaded with high (pathol.) levels of Ca2+, mitochondria become swollen and uncoupled as the result of a large non-specific increase in membrane permeability. This process, known as the mitochondrial permeability transition (MPT), is exacerbated by oxidative stress and adenine nucleotide depletion. These conditions match those that a **heart** experiences during **reperfusion** following a period of ischemia. The MPT is caused by the opening of a non-specific pore that can be prevented by sub-micromolar concns. of cyclosporin A (CsA). A variety of conditions that increase the sensitivity of pore opening to [Ca2+], such as thiol modification, oxidative stress, increased matrix vol. and chaotropic agents, all enhance the binding of matrix cyclophilin (CyP) to the inner mitochondrial membrane in a CsA-sensitive manner. In contrast, ADP, membrane potential and low pH decrease the sensitivity of pore opening to [Ca2+] without affecting CyP binding. We present a model of pore opening involving CyP binding to a membrane target protein followed by Ca2+-dependent triggering of a conformational change to induce channel opening. Using the ischemic/reperfused rat **heart** we have shown that the mitochondrial pore does not open during ischemia, but does do so during **reperfusion**. Recovery of **heart** during **reperfusion** is improved in the presence of 0.2 .mu.M CsA, suggesting that the MPT may be crit. in the transition from reversible to irreversible **reperfusion** injury.

ST **heart** ischemia **reperfusion** injury cyclophilin mitochondria

IT Membrane potential
(biol.; cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT Cell membrane
Conformation
Liver
Mitochondria
Oxidative stress, biological
Permeability
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT Calcium channel
Cyclophilins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT Thiols (organic), biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT **Reperfusion**
(injury; cyclosporin A binding to mitochondrial cyclophilin inhibits

the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT **Heart**, disease
(ischemia; cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT 7440-70-2, Calcium, biological studies
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT 58-64-0, 5'-ADP, biological studies 12408-02-5, Hydrogen ion, biological studies **59865-13-3**, Cyclosporin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

=> d l8 29 all

L8 ANSWER 29 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 126:338797 CA
TI Cardioprotection by cyclosporine A in experimental ischemia and **reperfusion** - evidence for a nitric oxide-dependent mechanism mediated by endothelin
AU Massoudy, P.; Zahler, S.; Kupatt, C.; Reder, E.; Becker, B. F.; Gerlach, E.
CS Dep. of Physiology and Dep. of Prophylaxis of Circulatory Diseases, Univ. of Munich, Germany
SO Journal of Molecular and Cellular Cardiology (1997), 29(2), 535-544
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic
DT Journal
LA English
CC 1-12 (Pharmacology)
AB The acute effect of cyclosporine A (CsA) on myocardial function after ischemia and **reperfusion** and the mechanism of action was investigated in isolated working guinea-pig hearts. Myocardial function was exptl. infringed by imposing short-term global ischemia and **reperfusion** (15 min each). External **heart** work (EHW), detd. before and after ischemia, served as the criterion for quantitation of recovery. Control hearts were perfused with modified Krebs-Henseleit buffer, other hearts received buffer supplemented with CsA .+-. an endothelin receptor antagonist or exogenous endothelin .+-. an inhibitor of nitric oxide (NO) synthesis. To assess the importance of endothelial prodn. of mediators directly, NO release in coronary effluent (continuously measured with an amperometric sensor) and release of 6-keto-prostaglandin F1.alpha. (6-keto-PGF1.alpha.), a stable metabolite of prostacyclin (PGI2), were detd. in non-working Langendorff hearts. Oxidative stress during **reperfusion** was assessed by measuring glutathione release in coronary venous effluent. Cyclosporine A (0.8 .mu.m) improved post-ischemic function significantly (59% recovery of EHW .upsilon. 31% for controls). At 0.08 .mu.m, CsA was without beneficial effect (30% recovery). The endothelin (ET)A- and ETB-receptor antagonist bosentan inhibited the protective action of 0.8 .mu.m CsA (32% recovery). Exogenous ET-1 (80 pm) improved recovery to 53%, an effect which was blocked by the inhibitor of NO-synthase, NG-nitroi-L-arginine (NOLAG, 1 .mu.m, 31% recovery). In the control group, post-ischemic NO release in

coronary effluent recovered from zero to about 100% of the pre-ischemic value by 10 min, but then decreased rapidly during the subsequent 15 min of **reperfusion**. In hearts treated with 0.8 .mu.m CsA, NO release stayed at 100% of the pre-ischemic value throughout **reperfusion**, the difference between controls and CsA-treated hearts being significant after 20 min of **reperfusion**. On the other hand, coronary venous release of 6-keto-PGF1.alpha. was not different between the groups. Release of glutathione during early **reperfusion** (first 5 min) was significantly lowered ($P<0.05$) to about 50% in CsA (0.8 .mu.m)- and ET-1-treated hearts as compared with controls (8.8 nmol/min). Cyclosporin A acts as a cardioprotective agent in our model of ischemia and **reperfusion**, presumably by elevating the level of endogenous nitric oxide and thereby reducing oxidative stress.

ST cyclosporine cardioprotective ischemia **reperfusion** NO endothelin

IT Cytoprotective agents
(cardioprotective; cyclosporine A cardioprotective effect in ischemia and **reperfusion**: nitric oxide-dependent mechanism mediated by endothelin)

IT Antioxidants
(cyclosporine A cardioprotective effect in ischemia and **reperfusion**: nitric oxide-dependent mechanism mediated by endothelin)

IT **Heart**, disease
(ischemia; cyclosporine A cardioprotective effect in ischemia and **reperfusion**: nitric oxide-dependent mechanism mediated by endothelin)

IT **59865-13-3**, Cyclosporine A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclosporine A cardioprotective effect in ischemia and **reperfusion**: nitric oxide-dependent mechanism mediated by endothelin)

IT 10102-43-9, Nitric oxide, biological studies 116243-73-3, Endothelin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporine A cardioprotective effect in ischemia and **reperfusion**: nitric oxide-dependent mechanism mediated by endothelin)

=> d 18 34 all

L8 ANSWER 34 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 113:71043 CA
TI Cyclosporin and mitochondrial dysfunction
AU McGuinness, Orla; Crompton, Martin
CS Dep. Biochem., Univ. Coll. London, London, WC1E 6BT, UK
SO Biochemical Society Transactions (1990), 18(5), 883-4
CODEN: BCSTB5; ISSN: 0300-5127
DT Journal
LA English
CC 1-8 (Pharmacology)
AB The potential of cyclosporin to protect against possible mitochondrial dysfunction during **reperfusion** was examd. The effects of Ca2+, O2, adenosine nucleotides, and cyclosporin on the inner membrane potential of rat liver mitochondria were studied. The adverse effects of Ca2+ and oxidative stress were abolished by 5 mM ATP. It may be concluded that the pathophysiol. free Ca2+ concn. likely to be encountered after prolonged ischemia, might well induce inner membrane pore opening when accompanied by high Pi concn. and oxidative stress, provided that cellular ATP is substantially depleted. The results also show that 0.6 .mu.m cyclosporin

allowed full development of .DELTA..psi. without added ATP, suggesting that cyclosporin may be of therapeutic value in halting the progression to irreversible injury during **reperfusion**.

ST cyclosporine mitochondria dysfunction ischemia **reperfusion**

IT Mitochondria
(dysfunction of, during **reperfusion** after ischemia, cyclosporin effect on)

IT Stress, biological
(oxidative, mitochondrial dysfunction during **reperfusion** after ischemia in relation to, cyclosporine effect on)

IT Ischemia
(**reperfusion** after, mitochondrial dysfunction from, cyclosporin effect on)

IT Perfusion
(re-, mitochondrial dysfunction after, of **heart**, cyclosporin protection against)

IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(mitochondrial dysfunction during **reperfusion** after ischemia in relation to, cyclosporine effect on)

IT 56-65-5, 5'-ATP, biological studies
RL: BIOL (Biological study)
(mitochondrial dysfunction during **reperfusion** after ischemia response to)

IT **79217-60-0**, Cyclosporin
RL: BIOL (Biological study)
(mitochondrial dysfunction response to, during **reperfusion** after ischemia)

IT 7782-44-7, Oxygen, biological studies
RL: BIOL (Biological study)
(stress from, mitochondrial dysfunction during **reperfusion** after ischemia in relation to, cyclosporine effect on)

=> d 18 33 all

L8 ANSWER 33 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 117:184589 CA
TI Impairment by cyclosporin A of **reperfusion**-induced arrhythmias
AU Arteaga, Diana; Odor, Alberto; Lopez, Rosa M.; Contreras, Gloria; Pichardo, Julieta; Garcia, Elizabeth; Aranda, Alberto; Chavez, Edmundo
CS Dep. Bioquim., Inst. Nac. Cardiol., Ignacio Chavez, Mex.
SO Life Sciences (1992), 51(14), 1127-34
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
CC 1-8 (Pharmacology)
AB This study introduces the immunosuppressant cyclosporin A as a cardioprotective drug. This effect was analyzed during development of **reperfusion**/induced arrhythmias after a 5-min period of coronary ligation in hearts of rats under anesthesia. The results indicate that cyclosporin A, when given before coronary occlusion, at a dose of 20 mg/kg, effectively protects against the high incidence of arrhythmias and the fall in blood pressure induced by **reperfusion**. In addn., it inhibits the delivery of lactic dehydrogenase and creatine kinase enzymes to the plasma. The authors propose that the protective effect could be related with its well documented action to restrain Ca2+-induced damage of mitochondrial functions.

ST cyclosporin A **heart** ischemia **reperfusion** antiarrhythmic

IT Antiarrhythmics
(cyclosporin A as, after **heart** ischemia and

reperfusion)
IT **Heart**, disease
(ischemia, **reperfusion** after, cyclosporin A treatment of, antiarrhythmic activity in)
IT Perfusion
(re-, after **heart** ischemia, cyclosporin A treatment of, antiarrhythmic activity in)
IT **59865-13-3**, Cyclosporin A
RL: BIOL (Biological study)
(**heart** ischemia and **reperfusion** treatment with, antiarrhythmic activity in)

=> d l8 32 all

L8 ANSWER 32 OF 35 CA COPYRIGHT 2003 ACS on STN
AN 120:153337 CA
TI Protection by cyclosporin A of ischemia/**reperfusion**-induced damage in isolated rat hearts
AU Griffiths, Elinor J.; Halestrap, Andrew P.
CS Sch. Med., Univ. Bristol, Bristol, BS8 1TD, UK
SO Journal of Molecular and Cellular Cardiology (1993), 25(12), 1461-9
CODEN: JMCDAY; ISSN: 0022-2828
DT Journal
LA English
CC 1-8 (Pharmacology)
AB **Reperfusion** following a period of ischemia can salvage the myocardium only if the ischemic episode has not exceeded a certain time limit; beyond this point damage becomes irreversible. A key feature of the transition from reversible to irreversible injury is mitochondrial dysfunction which may involve the opening of a non-specific pore in the mitochondrial inner membrane. Pore opening can be induced in vitro by exposure of isolated mitochondria to high [Ca2+] and Pi. Such pore formation is sensitized by adenine nucleotide depletion and oxidative stress and can be blocked by the immunosuppressant cyclosporin A. Here the authors show that in isolated perfused rat hearts subjected to 30 min ischemia and 15 min **reperfusion**, 0.2 .mu.M cyclosporin A restored the ATP/ADP ratio and AMP content (decreased and increased resp. during ischemia) to pre-ischemic values. In sep. expts. functional recovery was assessed by monitoring the restoration of left ventricular developed pressure (LVP) during **reperfusion** after 30, 40 or 45 min ischemia. LVP was substantially improved in the presence of 0.2 .mu.M cyclosporin A but did not return to pre-ischemic levels. The cyclosporin analogs G and H were less effective than cyclosporin A in protecting the **heart** during **reperfusion**. This is consistent with their reduced ability to protect isolated mitochondria from damage caused by Ca2+ overload. Surprisingly, **reperfusion** of hearts with 1 .mu.M cyclosporin A reversed the protective effect seen at 0.2 .mu.M.
ST cyclosporin A **heart** ischemia **reperfusion** injury; mitochondrion adenine nucleotide cyclosporin **heart** ischemia
IT Mitochondria
(adenine nucleotide depletion in **heart**, cyclosporin A prevention of, in ischemia/**reperfusion**-induced injury)
IT Nucleotides, biological studies
RL: BIOL (Biological study)
(adenine, of **heart** mitochondria, cyclosporin A effect on, in ischemia/**reperfusion**-induced injury prevention)
IT Perfusion
(re-, cyclosporin A protection against injury from ischemia and, mechanism of)
IT **Heart**, disease
(ventricle, ischemia, cyclosporin A protection against injury from, and

reperfusion, mechanism of)
IT 104987-11-3, FK-506
RL: BIOL (Biological study)
(**heart** protection by cyclosporin A vs., in ischemia/**reperfusion**-induced injury)
IT **59865-13-3**, Cyclosporin A **74436-00-3**, Cyclosporin G **83602-39-5**, Cyclosporin H
RL: BIOL (Biological study)
(**heart** protection by, in ischemia/**reperfusion**-induced injury, mechanism of)
IT 56-65-5, 5'-ATP, biological studies 58-64-0, ADP, biological studies 61-19-8, AMP, biological studies
RL: BIOL (Biological study)
(of **heart** mitochondria, cyclosporin A effect on, in ischemia/**reperfusion**-induced injury prevention)

```
=> d his

     (FILE 'HOME' ENTERED AT 11:09:56 ON 30 JUL 2003)

     FILE 'REGISTRY' ENTERED AT 11:10:07 ON 30 JUL 2003
                E CYCLOSPORINE
L1            0 S LE2-E3
L2         1255 S E2-E3

     FILE 'CA' ENTERED AT 11:11:28 ON 30 JUL 2003
L3            0 S L1
L4        13328 S L2
                E REPERFUSION
L5        20425 S E3
L6          124 S L5 AND L4
                E HEART
L7       266519 S E3
L8           35 S L7 AND L6

=> e transplant
E1            1     TRANSPLANER/BI
E2            1     TRANSPLANETARY/BI
E3        37843 --> TRANSPLANT/BI
E4            1     TRANSPLANTA/BI
E5            1     TRANSPLANTAATION/BI
E6            1     TRANSPLANTABILITIES/BI
E7          297     TRANSPLANTABILITY/BI
E8         4600     TRANSPLANTABLE/BI
E9            1     TRANSPLANTABLER/BI
E10           2     TRANSPLANTAION/BI
E11           1     TRANSPLANTAIONS/BI
E12           2     TRANSPLANTANT/BI

=> s e3-e8
          37843 TRANSPLANT/BI
              1 TRANSPLANTA/BI
              1 TRANSPLANTAATION/BI
              1 TRANSPLANTABILITIES/BI
            297 TRANSPLANTABILITY/BI
           4600 TRANSPLANTABLE/BI
L9        42398 (TRANSPLANT/BI OR TRANSPLANTA/BI OR TRANSPLANTAATION/BI OR TRANS
                PLANTABILITIES/BI OR TRANSPLANTABILITY/BI OR TRANSPLANTABLE/BI)

=> s l9 and l7
L10        5608 L9 AND L7
```

```
=> s l10 and l4
L11        858 L10 AND L4

=> s l11 and l5
L12         12 L11 AND L5

=> d l12 1-12

L12  ANSWER 1 OF 12  CA  COPYRIGHT 2003 ACS on STN
AN   138:385438  CA
TI   Preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as
     phosphodiesterase IV inhibitors.
IN   Eggenweiler, Hans-Michael; Wolf, Michael; Beier, Norbert; Schelling,
     Pierre; Ehring, Thomas
PA   Merck Patent Gmbh, Germany
SO   PCT Int. Appl., 114 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.   DATE
     ---------------    ----  --------       ---------------   --------
PI   WO 2003039548       A1   20030515       WO 2002-EP11351   20021010
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI EP 2001-125455    A    20011105
OS   MARPAT 138:385438
RE.CNT  4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12  ANSWER 2 OF 12  CA  COPYRIGHT 2003 ACS on STN
AN   137:352901  CA
TI   Preparation of substituted phenanthridinones as inhibitors of poly-ADP
     ribose synthase (PARS)
IN   Szabo, Csaba; Jagtap, Prakash; Southan, Garry; Salzman, Andrew
PA   Inotek Pharamaceuticals Corporation, USA
SO   U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 587,181, abandoned.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.         KIND  DATE           APPLICATION NO.   DATE
     ---------------    ----  --------       ---------------   --------
PI   US 6476048          B1   20021105       US 2000-602539    20000622
     US 6277990          B1   20010821       US 1999-454867    19991207
     WO 2001042219       A2   20010614       WO 2000-US42656   20001207
     WO 2001042219       A3   20011213
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
```

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1237871 A2 20020911 EP 2000-992673 20001207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 1999-454867 A2 19991207
US 2000-587181 B2 20000602
US 2000-602539 A2 20000622
US 2000-606587 A2 20000629
WO 2000-US42656 W 20001207
OS MARPAT 137:352901
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 135:352794 CA
TI Immunosuppressive compositions containing an immunophilin-binding compound and a ginkgolide compound, and screening method
IN Haines, David; Tosaki, Arpad; Mahmoud, Fadia F.
PA USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001085206	A2	20011115	WO 2001-US14718	20010508
WO 2001085206	A3	20021024		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1299119 A2 20030409 EP 2001-935128 20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-203110P P 20000508
WO 2001-US14718 W 20010508

L12 ANSWER 4 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 135:46112 CA
TI Synthesis and use of substituted phenanthridinones as inhibitors of poly-ADP ribose synthase (PARS)
IN Szabo, Csaba; Jagtap, Prakash; Southan, Garry; Salzman, Andrew L.
PA Inotek Corporation, USA
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001042219	A2	20010614	WO 2000-US42656	20001207
WO 2001042219	A3	20011213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US	6277990	B1	20010821	US 1999-454867	19991207
US	6476048	B1	20021105	US 2000-602539	20000622
US	6531464	B1	20030311	US 2000-606587	20000629
EP	1237871	A2	20020911	EP 2000-992673	20001207

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US	1999-454867	A2	19991207
US	2000-587181	A2	20000602
US	2000-602539	A2	20000622
US	2000-606587	A2	20000629
WO	2000-US42656	W	20001207

OS MARPAT 135:46112

L12 ANSWER 5 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 133:129866 CA
TI Methods using a CCR1 antagonist for preventing graft rejection and ischemia-**reperfusion** injury
IN Hancock, Wayne W.
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000044365	A1	20000803	WO 2000-US2123	20000127

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA	2360672	AA	20000803	CA 2000-2360672	20000127
EP	1152752	A1	20011114	EP 2000-907060	20000127

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP	2002535358	T2	20021022	JP 2000-595669	20000127
PRAI US	1999-239283	A2	19990129		
WO	2000-US2123	W	20000127		

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 132:160980 CA
TI Antisense oligodeoxynucleotides prevent acute cardiac allograft rejection via a novel, nontoxic, highly efficient transfection method
AU Poston, Robert S.; Mann, Michael J.; Hoyt, E. Grant; Ennen, Michael; Dzau, Victor J.; Robbins, Robert C.
CS Department of Cardiothoracic Surgery, Stanford University School of Medicine, Stanford, CA, 94305, USA

SO Transplantation (1999), 68(6), 825-832
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 132:59191 CA
TI Therapeutic methods employing disulfide derivatives of dithiocarbamates and compositions useful therefor
IN Lai, Ching-San; Vassilev, Vassil
PA Medinox, Inc., USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9966918	A1	19991229	WO 1999-US14237	19990622
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6093743	A	20000725	US 1998-103639	19980623
	CA 2335858	AA	19991229	CA 1999-2335858	19990622
	AU 9947119	A1	20000110	AU 1999-47119	19990622
	EP 1089723	A1	20010411	EP 1999-930617	19990622
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002518441	T2	20020625	JP 2000-555604	19990622
	US 6316502	B1	20011113	US 2000-565666	20000505
PRAI	US 1998-103639	A2	19980623		
	WO 1999-US14237	W	19990622		

OS MARPAT 132:59191
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 131:332966 CA
TI A process to study changes in gene expression in T lymphocytes
IN Prashar, Yatindra; Weissman, Sherman
PA Gene Logic, Inc., USA
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9957130	A1	19991111	WO 1999-US9761	19990505
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2326827	AA	19991111	CA 1999-2326827	19990505

AU 9938807 A1 19991123 AU 1999-38807 19990505
AU 759785 B2 20030501
EP 1075485 A1 20010214 EP 1999-921657 19990505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1998-84329P P 19980505
WO 1999-US9761 W 19990505
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 131:153752 CA
TI Modified pharmacologically active agents with cleavable thiocarbonyl sulfide substituent and improved therapeutic methods employing them
IN Lai, Ching-San
PA Medinox, Inc., USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9940787	A1	19990819	WO 1999-US2678	19990208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926627	A1	19990830	AU 1999-26627	19990208

PRAI US 1998-74694P A1 19980213
WO 1999-US2678 W 19990208
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 131:139497 CA
TI Methods for the controlled delivery of carbon disulfide for the treatment of inflammatory conditions
IN Lai, Ching-San
PA Medinox, Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9940907	A1	19990819	WO 1999-US2679	19990208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

AU 9926628 A1 19990830 AU 1999-26628 19990208
PRAI US 1998-74741P A1 19980213
WO 1999-US2679 W 19990208
OS MARPAT 131:139497
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 129:239628 CA
TI Effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure
AU Jurado, F.; Bellon, J. M.; Pareja, J. A.; Golitsin, A.; Millan, L.; Pascual, G.; Bujan, J.
CS Department of Morphological Sciences and Surgery (Surgical Research Laboratory), Faculty of Medicine, University of Alcala de Henares, Madrid, 28871, Spain
SO Histology and Histopathology (1998), 13(3), 761-774
CODEN: HIHIES; ISSN: 0213-3911
PB Histology and Histopathology
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 127:13451 CA
TI Triterpene derivatives with immunosuppressant activity, their preparation, and compositions containing them
IN Baker, Robert K.; Bao, Jianming; Kayser, Frank; Parsons, William H.; Rupprecht, Kathleen M.
PA Merck and Co., Inc., USA; Baker, Robert K.; Bao, Jianming; Kayser, Frank; Parsons, William H.; Rupprecht, Kathleen M.
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9716068	A1	19970509	WO 1996-US17211	19961028
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9674781	A1	19970522	AU 1996-74781	19961028
AU 712015	B2	19991028		
EP 877554	A1	19981118	EP 1996-937010	19961028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11514648	T2	19991214	JP 1996-517439	19961028
PRAI US 1995-8169		19951031		
US 1995-8189		19951031		
GB 1996-3833		19960223		
GB 1996-5156		19960312		
WO 1996-US17211		19961028		

OS MARPAT 127:13451

=> d his

(FILE 'HOME' ENTERED AT 11:09:56 ON 30 JUL 2003)

FILE 'REGISTRY' ENTERED AT 11:10:07 ON 30 JUL 2003
E CYCLOSPORINE
L1 0 S LE2-E3
L2 1255 S E2-E3

FILE 'CA' ENTERED AT 11:11:28 ON 30 JUL 2003
L3 0 S L1
L4 13328 S L2
E REPERFUSION
L5 20425 S E3
L6 124 S L5 AND L4
E HEART
L7 266519 S E3
L8 35 S L7 AND L6
E TRANSPLANT
L9 42398 S E3-E8
L10 5608 S L9 AND L7
L11 858 S L10 AND L4
L12 12 S L11 AND L5

=> s l12 not l8
L13 0 L12 NOT L8

=> d l12 11 all

L12 ANSWER 11 OF 12 CA COPYRIGHT 2003 ACS on STN
AN 129:239628 CA
TI Effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure
AU Jurado, F.; Bellon, J. M.; Pareja, J. A.; Golitsin, A.; Millan, L.; Pascual, G.; Bujan, J.
CS Department of Morphological Sciences and Surgery (Surgical Research Laboratory), Faculty of Medicine, University of Alcala de Henares, Madrid, 28871, Spain
SO Histology and Histopathology (1998), 13(3), 761-774
CODEN: HIHIES; ISSN: 0213-3911
PB Histology and Histopathology
DT Journal
LA English
CC 1-7 (Pharmacology)
Section cross-reference(s): 14
AB The present study investigates the effects on the cardiac muscle cell of 2 of the detg. factors for the success of organ **transplant**; ischemia-perfusion and immunosuppressive treatment with cyclosporin-A (CsA). To this end an abdominal, heterotopic **heart transplant** model in singenic Sprague-Dawley rats was employed. Three study groups were established: group I (control, n=15) animals undergoing **heart transplant** without treatment; group II (n=15) animals undergoing **heart transplant** and subjected to a daily dose of CsA in a cremophor vehicle (Sandimun) (5 mg/kg/s.c.); group III (n=15) animals undergoing **heart transplant** and administered a daily dose of pure CsA (5 mg/kg/s.c.). Recipient animals were sacrificed 7, 14, 21, 30, and 50 days after **transplant**. During the post-operative period, **heart** function was assessed by daily abdominal palpation. Graft specimens obtained at each follow-up period were subjected to light and transmission electron microscopy. Immunohistochem. anal. of specimens was performed using the rat macrophage-specific monoclonal antibody MCA-341. The ischemia/**reperfusion** process induced considerable alteration to cardiac muscle cells of control animals. Effects, apparent after the

1st week of **transplant**, included mitochondrial swelling and loss of cristae, hypertrophy of the sarcoplasmic reticulum and structural changes to sarcomeres. Two weeks after **transplant**, the myocardium was infiltrated by inflammatory cells. These effects diminished 30 days post-**transplant**. Cardiac tissues of treated animals (groups II and III) showed similar behavior although, in the latter group, mitochondrial damage was greater and intense myocardial fibrosis took place. Infiltration of cardiac muscle by white blood cells did not take place until 3 wk post-implant. These results indicate: a) The ultrastructural changes detected in cardiac fibers of animals of the 3 study groups were attributable to the ischemia/**reperfusion** process rather than to treatment with CsA; b) CsA appears to augment mitochondrial damage and myocardial fibrosis; c) the inflammatory response was delayed and reduced by the immunosuppressant; and d) the cremophor administration vehicle did not seem to exert an independent toxic effect on the myocardium.

ST cyclosporinA **heart transplant** ischemia **reperfusion** immunosuppressant

IT Immunosuppressants
(effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)

IT **Transplant** and Transplantation
(**heart**; effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)

IT **Reperfusion**
(injury; effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)

IT **Heart**
(**transplant**; effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)

IT 39279-69-1, Cremophor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of cyclosporin-A and its vehicle on cardiac muscle ultrastructure)

IT **59865-13-3**, Cyclosporin-A
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of ischemia-**reperfusion** and cyclosporin-A on cardiac muscle ultrastructure)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Abbott, C; Arch Surg 1964, V89, P645 MEDLINE
(2) Bakker, A; Histol Histopathol 1995, V10, P405 MEDLINE
(3) Bellon, J; J Biom Mater Res 1996, V31, P1 CA
(4) Bellon, J; Transplantation 1995, V60, P407 CA
(5) Bernier, M; Circ Res 1986, V58, P331 CA
(6) Bolli, R; J Am Coll Cardiol 1988, V12, P239 CA
(7) Braunwald, E; J Clin Invest 1985, V76, P1713 MEDLINE
(8) Cohen, D; Ann Intern Med 1984, V101, P667 CA
(9) de Caterina, R; Transplantation 1995, V60, P270 CA
(10) Del Maestro, R; Acta Physiol Scand (suppl) 1980, V492, P153 CA
(11) Engel, W; Nature 1961, V191, P389 MEDLINE
(12) Engler, R; Am J Physiol 1986, V251, P93
(13) Forman, M; J Am Coll Cardiol 1989, V13, P450 MEDLINE
(14) Fremes, S; J Thorac Cardiovasc Surg 1995, V110, P293 MEDLINE
(15) Garcia-Poblete, E; Histol Histopathol 1997, V12, P375 MEDLINE
(16) Guttmann, R; Transplant Proc 1994, V5, P2564
(17) Homan, W; Transplantation 1980, V30, P354 CA
(18) Hutcheson, A; Res Commun Mol Pathol Pharmacol 1995, V89, P17 CA
(19) Jeevanandam, V; J Thorac Cardiovasc Surg 1992, V104, P224 MEDLINE

(20) Kahan, B; Transplantation 1985, V40, P457 CA
(21) Karch, S; J Heart Transplant 1985, V4, P210 MEDLINE
(22) Klintmalm, G; Transplantation 1981, V32, P488 MEDLINE
(23) Luke, R; J Clin Invest 1991, V87, P1594 MEDLINE
(24) Mason, J; Pharmacol Rev 1984, V41, P423
(25) Meiser, B; Lancet 1991, V338, P1297 MEDLINE
(26) Menasche, P; J Thorac Cardiovasc Surg 1993, V105, P353 MEDLINE
(27) Millane, T; J Heart Lung Transplant 1994, V13, P473 MEDLINE
(28) Morris, P; Transplant Proc 1983, V15, P2287 CA
(29) Ono, K; J Thorac Cardiovasc Surg 1969, V57, P225 MEDLINE
(30) Paul, L; Transplantation 1994, V57, P1767 MEDLINE
(31) Pesonen, E; J Thorac Cardiovasc Surg 1995, V110, P768 MEDLINE
(32) Severs, N; Electron Microscopy 92, Eurem 92 1992, V1, P627
(33) Severs, N; Histol Histopathol 1995, V10, P481 MEDLINE
(34) Smith, J; Am J Pathol 1991, V139, P801 MEDLINE
(35) Stringham, J; J Thorac Cardiovasc Surg 1994, V107, P764 MEDLINE
(36) Tatou, E; Pharmacology 1996, V52, P1 CA
(37) Tauber, J; Transplantation 1978, V26, P409 MEDLINE
(38) Thomson, A; Immunology 1983, V48, P301 CA
(39) Uretsky, B; Circulation 1987, V76, P827 MEDLINE
(40) Wish, J; Transplant Proc 1986, V18(suppl 2), P15

=> d hsi
L13 HAS NO ANSWERS
L2 1255 SEA FILE=REGISTRY (CYCLOSPORIN/BI OR CYCLOSPORINE/BI)
L4 13328 SEA FILE=CA L2
L5 20425 SEA FILE=CA REPERFUSION/BI
L6 124 SEA FILE=CA L5 AND L4
L7 266519 SEA FILE=CA HEART/BI
L8 35 SEA FILE=CA L7 AND L6
L9 42398 SEA FILE=CA (TRANSPLANT/BI OR TRANSPLANTA/BI OR TRANSPLANTAATIO
N/BI OR TRANSPLANTABILITIES/BI OR TRANSPLANTABILITY/BI OR
TRANSPLANTABLE/BI)
L10 5608 SEA FILE=CA L9 AND L7
L11 858 SEA FILE=CA L10 AND L4
L12 12 SEA FILE=CA L11 AND L5
L13 0 SEA FILE=CA L12 NOT L8

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	93.95	111.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.58	-5.58

STN INTERNATIONAL LOGOFF AT 11:29:56 ON 30 JUL 2003

AN 130:261685 CA
TI Cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury in rats
AU Squadrito, Francesco; Altavilla, Domenica; Squadrito, Giovanni; Saitta, Antonino; Campo, Giuseppe M.; Arlotta, Mariarita; Quartarone, Cristina; Ferlito, Marcella; Caputi, Achille P.
CS Institute of Pharmacology, School of Medicine, University of Messina, Messina, 98121, Italy
SO European Journal of Pharmacology (1999), 364(2/3), 159-168
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-7 (Pharmacology)
AB The present study was designed to evaluate the effect of cyclosporin A in a rat model of myocardial ischemia-**reperfusion** injury (MI/R). Anesthetized rats were subjected to total occlusion (20 min) of the left main coronary artery followed by 5 h **reperfusion** (MI/R). Sham myocardial ischemia-**reperfusion** rats (Sham MI/R) were used as controls. Myocardial necrosis, myocardial myeloperoxidase activity (MPO), serum creatinine phosphokinase activity (CPK), serum tumor necrosis factor (TNF-.alpha.), cardiac mRNA for TNF-.alpha., cardiac intercellular adhesion mol.-1 (ICAM-1) immunostaining, and myocardial contractility (left ventricle dP/dtmax) were evaluated. Myocardial ischemia plus **reperfusion** in untreated rats produced marked myocardial necrosis, increased serum CPK activity and myeloperoxidase activity (a marker of leukocyte accumulation) both in the area-at-risk and in the necrotic area, reduced myocardial contractility, and induced a marked increase in the serum levels of the TNF-.alpha.. Furthermore, increased cardiac mRNA for TNF-.alpha. was measurable within 10-20 min of left main coronary artery occlusion in the area-at-risk and increased levels were generally sustained for 0.5 h. Finally, myocardial ischemia-**reperfusion** injury increased ICAM-1 staining in the myocardium. The administration of cyclosporin A (0.25, 0.5, and 1 mg/kg as an i.v. infusion 5 min after coronary artery occlusion) lowered myocardial necrosis and myeloperoxidase activity in the area-at-risk and in the necrotic area, decreased serum CPK activity, increased myocardial contractility, reduced serum levels of TNF-.alpha. and the cardiac cytokine mRNA levels, and blunted ICAM-1 immunostaining in the injured myocardium. The data suggest that cyclosporin A suppresses leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury.
ST cyclosporin A leukocyte accumulation; myocardial ischemia **reperfusion** injury cyclosporin A
IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT Immunosuppression
Leukocyte
Reperfusion
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT Immunoassay
(immunol. staining; cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)

IT **Heart**, disease
(infarction; cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT **Heart**, disease
(ischemia; cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT 9001-15-4, Creatinine phosphokinase 9003-99-0, Myeloperoxidase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
IT **59865-13-3**, Cyclosporin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclosporin A reduces leukocyte accumulation and protects against myocardial ischemia-**reperfusion** injury)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Arbustini, E; Am J Cardiol 1991, V68, P368
(2) Braquet, P; Pharmacol Rev 1987, V39, P97 CA
(3) Chung, M; Circ Res 1990, V67, P753 CA
(4) Clipstone, N; Ann New York Acad Sci 1993, V696, P20 CA
(5) Coker, S; Br J Pharmacol 1985, V86, P259 CA
(6) Collart, M; Mol Cell Biol 1990, V10, P1498 CA
(7) Dzau, V; Circ Res 1993, V16(Suppl II), PII5
(8) Feuerstein, G; Prostaglandin 1984, V27, P781 CA
(9) Finkel, M; Science 1992, V257, P387 CA
(10) Fruman, D; Immunosuppressive Drugs:Developments in Anti-rejection Therapy 1994, P15
(11) Hirsh, A; Circ Res 1991, V69, P475
(12) Hsu, S; Am J Clin Pathol 1981, V75, P734 CA
(13) Klein, H; Arch Pathol Anat 1981, V393, P287 CA
(14) Lucchesi, B; Annu Rev Physiol 1990, V52, P561 CA
(15) Massoudy, P; J Mol Cell Cardiol 1977, V29, P535
(16) McCord, J; New Engl J Med 1985, V312, P159 CA
(17) McMurray, J; Br Heart J 1991, V66, P356 MEDLINE
(18) Mullane, K; J Pharmacol Methods 1985, V14, P156
(19) Schreck, R; Free Radic Res Commun 1992, V17, P221 CA
(20) Schunkert, R; J Clin Invest 1990, V86, P1913
(21) Seekamp, A; Am J Pathol 1993, V143, P464 CA
(22) Seekamp, A; Am J Pathol 1994, V144, P592 CA
(23) Shandelya, S; Circulation 1993, V88, P2812 CA
(24) Squadrito, F; Eur J Pharmacol 1993, V273, P223
(25) Squadrito, F; Inflamm Res 1996, V45, P14 CA
(26) Squadrito, F; Life Sci 1993, V53, P341 CA
(27) van der Poll, T; Shock 1995, V3, P1 MEDLINE
(28) Wiederrecht, G; Ann New York Acad Sci 1993, V696, P9 CA
(29) Wu, C; Transplantation 1990, V54, P326
(30) Yamada, T; Circulation 1994, V89, P846 CA

=>

AN 129:156700 CA
TI Cyclosporine A limits myocardial infarct size even when administered after onset of ischemia
AU Weinbrenner, Christof; Liu, Guang S.; Downey, James M.; Cohen, Michael V.
CS University of South Alabama, MSB 3050, Departments of Physiology and Medicine, College of Medicine, Mobile, AL, 36688, USA
SO Cardiovascular Research (1998), 38(3), 676-684
CODEN: CVREAU; ISSN: 0008-6363
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-8 (Pharmacology)
AB The effects of the immunosuppressant drug cyclosporin A (CsA) as a preconditioning mimetic were examd. in rabbit hearts. CsA, a potent protein 2B or calcium/calmodulin-dependent phosphatase (PP) inhibitor, was administered to isolated rabbit hearts starting either 15 min prior to or 10 or 20 min after the onset of a 30-min regional ischemia and continuing until the onset of **reperfusion**. The effects of pretreatment with another PP2B antagonist, FK-506, were also examd. In an addnl. expt. NG-nitro-L-arginine Me ester (L-NAME) was perfused for 50 min starting 5 min before the 45-min infusion of CsA. After 2 h of **reperfusion** the infarction size was measured with the triphenyltetrazolium chloride method. In the second study, left ventricular biopsies of isolated rabbit hearts were obtained to measure the effects of CsA on the dephosphorylation of [32P]phosphorylase kinase by calcium/calmodulin-dependent phosphatases. Pretreatment with CsA resulted in only 10% infarction in the risk zone, significantly less than in untreated controls (28.7%), but comparable to the extent of infarction in ischemia preconditioned hearts (10%). Equivalent protection was also obsd. in hearts with treatment delayed for 10 min following the onset of ischemia (10.4% infarction). The protection waned when CsA was given only during the last 10 min of the 30-min ischemic period (25.5% infarction). Pretreatment with FK-506 also resulted in myocardial salvage (10.4% infarction). When the hearts were exposed to a coinfusion of L-NAME and CsA, the protection was still evident (18.1% infarction), although not as robustly as with the PP2B blocker alone. In hearts pretreated with CsA the dephosphorylation of [32P]phosphorylase kinase by calcium/calmodulin-dependent phosphatases was inhibited by 67%. Thus, CsA and FK-506, potent PP2B inhibitors, can protect the ischemic rabbit **heart**. CsA continues to be effective when its infusion is delayed until after the onset of **heart** ischemia. The mechanism of this protection may be related to the inhibition of phosphatases and prolongation of the phosphorylation state of ischemic cells.
ST **heart** ischemia infarction cyclosporine FK506 nitroarginine
IT **Heart**, disease
(infarction; cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)
IT **Heart**, disease
(ischemia; cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)
IT 50903-99-6, L-Name **59865-13-3**, Cyclosporin A 104987-11-3, Tacrolimus
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)
IT 9001-88-1, Phosphorylase kinase 9025-75-6, Protein phosphatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A, FK-506 and L-NAME effects on myocardial infarction size in isolated guinea pig ischemic hearts)
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Armstrong, S; J Mol Cell Cardiol 1992, V24, P869 CA
(2) Armstrong, S; J Mol Cell Cardiol 1996, V28, P1479 CA
(3) Armstrong, S; J Mol Cell Cardiol 1997, V29, P3009 CA
(4) Banerjee, A; Circ Res 1993, V73, P656 CA
(5) Bilinska, M; Mol Cell Biochem 1996, V160, P265
(6) Brunner, F; J Mol Cell Cardiol 1992, V24, P1291 CA
(7) Bunchman, T; J Clin Invest 1991, V88, P310 CA
(8) Caroni, P; Soc Gen Physiol Ser 1984, V38, P149 CA
(9) Clipstone, N; Nature 1992, V357, P695 CA
(10) Cohen, M; Cardiovasc Res 1994, V28, P61 MEDLINE
(11) Crompton, M; Biochem J 1988, V255, P357 CA
(12) Duchen, M; Cardiovasc Res 1993, V27, P1790 CA
(13) Fahr, A; Clin Pharmacokinet 1993, V24, P472 MEDLINE
(14) Fruman, D; Proc Natl Acad Sci USA 1992, V89, P3686 CA
(15) Fukuda, H; Biochem Biophys Res Commun 1996, V220, P160 CA
(16) Gabauer, I; Can J Cardiol 1994, V10, P125 CA
(17) Ganapathi, M; Arch Biochem Biophys 1984, V233, P19 CA
(18) Goodall, T; J Cardiovasc Pharmacol 1995, V26(Suppl 3), PS482
(19) Goto, M; Cardiovasc Res 1991, V25, P943 CA
(20) Goto, M; Circ Res 1995, V77, P611 CA
(21) Griffiths, E; Biochem J 1991, V274, P611 CA
(22) Griffiths, E; Biochem J 1995, V307, P93 CA
(23) Griffiths, E; J Mol Cell Cardiol 1993, V25, P1461 CA
(24) Groblewski, G; J Biol Chem 1994, V269, P15111 CA
(25) Ikonomidis, J; Am J Physiol 1997, V272, PH1220 CA
(26) Kahan, B; New Engl J Med 1989, V321, P1725 CA
(27) Klee, C; Methods Enzymol 1983, V102, P227 CA
(28) Laemmli, U; Nature 1970, V227, P680 CA
(29) Linden, J; Trends Pharmacol Sci 1994, V15, P298 CA
(30) Liu, G; Circulation 1991, V84, P350 CA
(31) Liu, J; Cell 1991, V66, P807 CA
(32) Liu, Y; Cardiovasc Drugs Ther 1994, V8, P881 MEDLINE
(33) Liu, Y; Circ Res 1996, V78, P443 CA
(34) Liu, Y; J Mol Cell Cardiol 1995, V27, P883 CA
(35) Massoudy, P; J Mol Cell Cardiol 1997, V29, P535 CA
(36) Maxwell, M; Cardiovasc Res 1987, V21, P737 MEDLINE
(37) Murry, C; Circulation 1986, V74, P1124 MEDLINE
(38) Schreiber, S; Immunol Today 1992, V13, P136 CA
(39) Schultz, J; Am J Physiol 1995, V268, PH2157 CA
(40) Speechly-Dick, M; Circ Res 1994, V75, P586 CA
(41) Stewart, A; Eur J Biochem 1981, V115, P197 CA
(42) Stewart, A; Eur J Biochem 1983, V132, P289 CA
(43) Stewart, A; FEBS Lett 1982, V137, P80 CA
(44) Stewart, A; Methods Enzymol 1988, V159, P409 CA
(45) Takeda, Y; J Cardiovasc Pharmacol 1993, V22(Suppl 8), PS310
(46) Taniguchi, I; J Mol Cell Cardiol 1997, V29, PA232
(47) Thornton, J; Circulation 1992, V85, P659 CA
(48) Thornton, J; J Mol Cell Cardiol 1993, V25, P311 CA
(49) Tsuchida, A; Circ Res 1994, V75, P576 CA
(50) Vander, H; Cardiovasc Res 1996, V31, P711
(51) Walsh, A; FEBS Lett 1997, V416, P230 CA
(52) Walsh, C; J Biol Chem 1992, V267, P13115 CA
(53) Wang, P; Basic Res Cardiol 1996, V91, P458 MEDLINE
(54) Wang, P; J Mol Cell Cardiol 1996, V28, P579 CA
(55) Weinbrenner, C; Circulation, in press 1998
(56) Weinbrenner, C; J Mol Cell Cardiol 1997, V29, P2383 CA
(57) Wera, S; Biochem J 1995, V311, P17 CA
(58) Weselcouch, E; Am J Physiol 1995, V268, PH242 CA
(59) Wolf, H; Proc Natl Acad Sci USA 1980, V77, P5852 CA
(60) Woolfson, R; Circulation 1995, V91, P1545 CA
(61) Yang, X; J Mol Cell Cardiol 1997, V29, P991 CA

(62) Yao, Z; Am J Physiol 1993, V264, PH2221 CA
(63) Ytrehus, K; Am J Physiol 1994, V266, PH1145 CA
(64) Zimmermann, N; Transplant Proc 1994, V26, P2875 CA

=>

AN 127:306090 CA
TI Cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury
AU Halestrap, A. P.; Connern, C. P.; Griffiths, E. J.; Kerr, P. M.
CS Departments of Biochemistry and Cardiac Surgery, University of Bristol, Bristol, BS8 ITD, UK
SO Molecular and Cellular Biochemistry (1997), 174(1&2), 167-172
CODEN: MCBIB8; ISSN: 0300-8177
PB Kluwer
DT Journal
LA English
CC 14-5 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
AB When loaded with high (pathol.) levels of Ca2+, mitochondria become swollen and uncoupled as the result of a large non-specific increase in membrane permeability. This process, known as the mitochondrial permeability transition (MPT), is exacerbated by oxidative stress and adenine nucleotide depletion. These conditions match those that a **heart** experiences during **reperfusion** following a period of ischemia. The MPT is caused by the opening of a non-specific pore that can be prevented by sub-micromolar concns. of cyclosporin A (CsA). A variety of conditions that increase the sensitivity of pore opening to [Ca2+], such as thiol modification, oxidative stress, increased matrix vol. and chaotropic agents, all enhance the binding of matrix cyclophilin (CyP) to the inner mitochondrial membrane in a CsA-sensitive manner. In contrast, ADP, membrane potential and low pH decrease the sensitivity of pore opening to [Ca2+] without affecting CyP binding. We present a model of pore opening involving CyP binding to a membrane target protein followed by Ca2+-dependent triggering of a conformational change to induce channel opening. Using the ischemic/reperfused rat **heart** we have shown that the mitochondrial pore does not open during ischemia, but does do so during **reperfusion**. Recovery of **heart** during **reperfusion** is improved in the presence of 0.2 .mu.M CsA, suggesting that the MPT may be crit. in the transition from reversible to irreversible **reperfusion** injury.
ST **heart** ischemia **reperfusion** injury cyclophilin mitochondria
IT Membrane potential
(biol.; cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)
IT Cell membrane
Conformation
Liver
Mitochondria
Oxidative stress, biological
Permeability
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)
IT Calcium channel
Cyclophilins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)
IT Thiols (organic), biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT **Reperfusion**
(injury; cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT **Heart**, disease
(ischemia; cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT 7440-70-2, Calcium, biological studies
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

IT 58-64-0, 5'-ADP, biological studies 12408-02-5, Hydrogen ion, biological studies **59865-13-3**, Cyclosporin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporin A binding to mitochondrial cyclophilin inhibits the permeability transition pore and protects hearts from ischemia/ **reperfusion** injury)

=>

AN 117:184589 CA
TI Impairment by cyclosporin A of **reperfusion**-induced arrhythmias
AU Arteaga, Diana; Odor, Alberto; Lopez, Rosa M.; Contreras, Gloria; Pichardo, Julieta; Garcia, Elizabeth; Aranda, Alberto; Chavez, Edmundo
CS Dep. Bioquim., Inst. Nac. Cardiol., Ignacio Chavez, Mex.
SO Life Sciences (1992), 51(14), 1127-34
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
CC 1-8 (Pharmacology)
AB This study introduces the immunosuppressant cyclosporin A as a cardioprotective drug. This effect was analyzed during development of **reperfusion**/induced arrhythmias after a 5-min period of coronary ligation in hearts of rats under anesthesia. The results indicate that cyclosporin A, when given before coronary occlusion, at a dose of 20 mg/kg, effectively protects against the high incidence of arrhythmias and the fall in blood pressure induced by **reperfusion**. In addn., it inhibits the delivery of lactic dehydrogenase and creatine kinase enzymes to the plasma. The authors propose that the protective effect could be related with its well documented action to restrain Ca2+-induced damage of mitochondrial functions.
ST cyclosporin A **heart** ischemia **reperfusion** antiarrhythmic
IT Antiarrhythmics
(cyclosporin A as, after **heart** ischemia and **reperfusion**)
IT **Heart**, disease
(ischemia, **reperfusion** after, cyclosporin A treatment of, antiarrhythmic activity in)
IT Perfusion
(re-, after **heart** ischemia, cyclosporin A treatment of, antiarrhythmic activity in)
IT **59865-13-3**, Cyclosporin A
RL: BIOL (Biological study)
(**heart** ischemia and **reperfusion** treatment with, antiarrhythmic activity in)

=>

AN 113:71043 CA
TI Cyclosporin and mitochondrial dysfunction
AU McGuinness, Orla; Crompton, Martin
CS Dep. Biochem., Univ. Coll. London, London, WC1E 6BT, UK
SO Biochemical Society Transactions (1990), 18(5), 883-4
CODEN: BCSTB5; ISSN: 0300-5127
DT Journal
LA English
CC 1-8 (Pharmacology)
AB The potential of cyclosporin to protect against possible mitochondrial dysfunction during **reperfusion** was examd. The effects of Ca2+, O2, adenosine nucleotides, and cyclosporin on the inner membrane potential of rat liver mitochondria were studied. The adverse effects of Ca2+ and oxidative stress were abolished by 5 mM ATP. It may be concluded that the pathophysiol. free Ca2+ concn. likely to be encountered after prolonged ischemia, might well induce inner membrane pore opening when accompanied by high Pi concn. and oxidative stress, provided that cellular ATP is substantially depleted. The results also show that 0.6 .mu.m cyclosporin allowed full development of .DELTA..psi. without added ATP, suggesting that cyclosporin may be of therapeutic value in halting the progression to irreversible injury during **reperfusion**.
ST cyclosporine mitochondria dysfunction ischemia **reperfusion**
IT Mitochondria
(dysfunction of, during **reperfusion** after ischemia, cyclosporin effect on)
IT Stress, biological
(oxidative, mitochondrial dysfunction during **reperfusion** after ischemia in relation to, cyclosporine effect on)
IT Ischemia
(**reperfusion** after, mitochondrial dysfunction from, cyclosporin effect on)
IT Perfusion
(re-, mitochondrial dysfunction after, of **heart**, cyclosporin protection against)
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(mitochondrial dysfunction during **reperfusion** after ischemia in relation to, cyclosporine effect on)
IT 56-65-5, 5'-ATP, biological studies
RL: BIOL (Biological study)
(mitochondrial dysfunction during **reperfusion** after ischemia response to)
IT **79217-60-0**, Cyclosporin
RL: BIOL (Biological study)
(mitochondrial dysfunction response to, during **reperfusion** after ischemia)
IT 7782-44-7, Oxygen, biological studies
RL: BIOL (Biological study)
(stress from, mitochondrial dysfunction during **reperfusion** after ischemia in relation to, cyclosporine effect on)

=>